Page 1 of 8





ENTERED

OIPE

RAW SEQUENCE LISTING

PATENT APPLICATION: US/10/025,514

DATE: 04/22/2002 TIME: 16:20:21

Input Set : A:\36829-20002.00.txt

Output Set: N:\CRF3\04222002\J025514.raw

```
4 <110> APPLICANT: Philip J. BARR
             Helen GIBSON
      5
             Philip PEMBERTON
      6
     8 <120> TITLE OF INVENTION: MULTIFUNCTIONAL PROTEASE INHIBITORS AND
             THEIR USE IN TREATMENT OF DISEASE
     12 <130> FILE REFERENCE: 368292000200
C--> 14 <140> CURRENT APPLICATION NUMBER: US/10/025,514
C--> 15 <141> CURRENT FILING DATE: 2002-04-03
     17 <150> PRIOR APPLICATION NUMBER: U.S. 60/256,699
     18 <151> PRIOR FILING DATE: 2000-12-18
     20 <150> PRIOR APPLICATION NUMBER: U.S. 60/331,966
     21 <151> PRIOR FILING DATE: 2001-11-20
     23 <160> NUMBER OF SEQ ID NOS: 33
     25 <170> SOFTWARE: FastSEQ for Windows Version 4.0
     27 <210> SEQ ID NO: 1
     28 <211> LENGTH: 1182
     29 <212> TYPE: DNA
     30 <213> ORGANISM: Homo sapiens
     32 <400> SEQUENCE: 1
     33 gaagaccete aaggegaege egeteaaaaa aeegaeacea gteateaega eeaagaeeat
                                                                                 60
     34 ccgactttta ataaaattac tccaaattta gccgaatttg ctttttcttt gtatagacaa
                                                                               120
     35 ttagctcatc aaagtaattc tactaacatt ttttttagtc ctgtttctat tgccactgct
                                                                               180
     36 ttcgccatgt tgagtttagg tactaaagcc gatacccatg acgagatttt agaaggttta
                                                                               240
     37 aactttaatt tgaccgaaat cccagaagcc caaattcacg agggttttca agagttgttg
                                                                               300
     38 agaactttga atcaacctga ttctcaattg caattaacta ctggtaacgg tttatttttg
                                                                                360
     39 tctgaaggtt taaaattggt tgacaaattc ctagaagacg tcaagaaact atatcatagt
                                                                                420
     40 gaggetttta eegttaattt tggtgataet gaggaageta aaaageaaat taatgattat
                                                                                480
     41 gttgagaaag gcacccaggg taagatcgtt gacctagtta aagaattaga tcgtgatacc
                                                                                540
     42 gtcttcgcac tagttaacta tattttttc aagggtaagt gggaacgtcc tttcgaggtt
                                                                                600
     43 aaagatactg aagaggaaga ttttcatgtt gatcaagtta ctactgtcaa agttccaatg
                                                                                660
     44 atgaaaagac tgggtatgtt caatattcaa cattgcaaaa aattaagttc ttgggtctta
                                                                                720
     45 ttaatgaagt atttaggtaa cgctactgct atttttttt taccagacga aggtaagctt
                                                                                780
     46 caacatttag agaatgagtt gactcatgac attattacta aatttttaga gaacgaggat
                                                                                840
     47 cgtcgtagcg cttctctgca cctgccaaag ttaagtatca ccggtactta cgacttaaaa
                                                                                900
     48 tctgttttag gccagttagg tattaccaaa gttttttcta acggtgccga tttgagtggt
                                                                                960
     49 gttactgaag aagctccatt aaaattgagt aaagctgttc acaaagccgt cttaactatt
                                                                               1020
     50 gatgaaaagg gtaccgaggc cgccggcgct atgttcctgg aagctattcc aatgagcatt
                                                                               1080
     51 ccaccagaag ttaaatttaa taaaccattc gtttttctga tgatcgagca gaacactaaa
                                                                               1140
                                                                               1182
     52 agcccattgt ttatgggtaa ggttgtcaac ccaactcaga ag
     54 <210> SEQ ID NO: 2
     55 <211> LENGTH: 394
     56 <212> TYPE: PRT
```

57 <213> ORGANISM: Homo sapiens

Input Set : A:\36829-20002.00.txt

| 59 <400> SEQUENCE: | 2 | | | • | mb-m | Com ! | Jie Wie |
|---|---------------|------------------|---------|----------------|---------------|------------|----------------|
| 60 Glu Asp Pro Gln | Gly Asp | | | | | | |
| 61 1 62 Asp Gln Asp His | Pro Thr | | | | | | |
| 63 20 64 Phe Ala Phe Ser | | | Leu A | | | | |
| 65 35 66 Asn Ile Phe Phe | | Val Ser | | | | | |
| 67 50 68 Ser Leu Gly Thr | Lys Ala | 55 Asp Thr | His A | sp Glu 75 | Ile Leu | Glu | Gly Leu 80 |
| 69 65 70 Asn Phe Asn Leu | 70 Thr Glu | Ile Pro | Glu A | la Gln | Ile His | Glu | Gly Phe 95 |
| 71 72 Gln Glu Leu Leu | 85 Arg Thr | Leu Asn | Gln P | ro Asp | Ser Glr | Leu 110 | Gln Leu |
| 73 100 74 Thr Thr Gly Asn | Gly Leu | Phe Leu | Ser G | Glu Gly | Leu Lys | Leu | Val Asp |
| 75 115 76 Lys Phe Leu Glu | | Lys Lys | | | | | |
| 77 130 78 Val Asn Phe Gly | Asp Thr | Glu Glu | ı Ala I | Lys Lys 155 | Gln Ile | e Asn | Asp Tyr 160 |
| 79 145 80 Val Glu Lys Gly | Thr Glr | | s Ile V | Val Asp | | | |
| 81 82 Asp Arg Asp Thi | | | ı Val A | | | | |
| 83 180 84 Lys Trp Glu Arg | | e Glu Va | l Lys i | | | u Glu | |
| 85 195 86 His Val Asp Gl | | z Thr Va | | | | | |
| 87 210 88 Gly Met Phe As | n Ile Gl | n His Cy | | | Ser Se | | |
| 89 225 90 Leu Met Lys Ty | | | a Thr | Ala Ile | | | |
| 91 92 Glu Gly Lys Le | | | u Asn | | | | |
| 93 26 94 Thr Lys Phe Le | | | | | Ala Se | er Leu | |
| 95 275 96 Pro Lys Leu Se | | | | | ı Lys Se | | |
| 97 290 98 Gln Leu Gly Il | | | | | | | |
| 99 305 100 Val Thr Glu G | | | | | | | |
| | | | | | | | |
| 101 102 Val Leu Thr 1 103 | | | | | | | |
| 103 104 Leu Glu Ala 3 105 355 | | | | | | | |
| 105 355 106 Pro Phe Val 1 107 370 | Phe Leu l | Met Ile (375 | Glu Glı | n Asn T | hr Lys 380 | Ser P | ro Leu Phe |

Input Set : A:\36829-20002.00.txt

```
108 Met Gly Lys Val Val Asn Pro Thr Gln Lys
                        390
109 385
111 <210> SEQ ID NO: 3
112 <211> LENGTH: 321
113 <212> TYPE: DNA
114 <213> ORGANISM: Homo sapiens
116 <400> SEQUENCE: 3
117 totggaaagt otttoaaggo oggtgtttgt ocaccaaaga agtoogotoa atgtttgaga
                                                                             60
118 tacaagaage cagaatgtca atccgactgg caatgtccag gtaagaagag atgttgtcca
                                                                            120
119 gacacttgtg gtatcaagtg tctagaccca gttgacaccc caaacccaac tagaagaaag
                                                                            180
120 ccaggtaagt gtccagttac ttacggtcaa tgtttgatgt tgaacccacc aaacttctgt
                                                                            240
121 gaaatggacg gtcaatgtaa gagagacttg aagtgttgta tgggtatgtg tggtaagtcc
                                                                            300
                                                                             321
122 tgtgtttccc cagtcaaggc c
124 <210> SEQ ID NO: 4
125 <211> LENGTH: 107
126 <212> TYPE: PRT
 127 <213> ORGANISM: Homo sapiens
 129 <400> SEQUENCE: 4
 130 Ser Gly Lys Ser Phe Lys Ala Gly Val Cys Pro Pro Lys Lys Ser Ala
                                          10
                      5
 132 Gln Cys Leu Arg Tyr Lys Lys Pro Glu Cys Gln Ser Asp Trp Gln Cys
                                      25
                 20
 134 Pro Gly Lys Lys Arg Cys Cys Pro Asp Thr Cys Gly Ile Lys Cys Leu
                                  40
 136 Asp Pro Val Asp Thr Pro Asn Pro Thr Arg Arg Lys Pro Gly Lys Cys
             35
 135
                                                  60
                              55
         50
 138 Pro Val Thr Tyr Gly Gln Cys Leu Met Leu Asn Pro Pro Asn Phe Cys
                                              75
                          70
 140 Glu Met Asp Gly Gln Cys Lys Arg Asp Leu Lys Cys Cys Met Gly Met
                                          90
                      85
 141
 142 Cys Gly Lys Ser Cys Val Ser Pro Val Lys Ala
                                      105
                 100
 143
 145 <210> SEQ ID NO: 5
 146 <211> LENGTH: 552
 147 <212> TYPE: DNA
 148 <213> ORGANISM: Homo sapiens
 150 <400> SEQUENCE: 5
 151 tgcacctgtg teccaeecca eccaeagaeg geettetgea atteegaeet egteateagg
                                                                               60
 152 gccaagttcg tggggacacc agaagtcaac cagaccacct tataccagcg ttatgagatc
                                                                              120
 153 aagatgacca agatgtataa agggttccaa gccttagggg atgccgctga catccggttc
                                                                              180
 154 gtctacaccc ccgccatgga gagtgtctgc ggatacttcc acaggtccca caaccgcagc
                                                                              240
  155 gaggagtttc tcattgctgg aaaactgcag gatggactct tgcacatcac tacctgcagt
                                                                              300
                                                                              360
  156 ttcgtggctc cctggaacag cctgagctta gctcagcgcc ggggcttcac caagacctac
  157 actgttggct gtgaggaatg cacagtgttt ccctgtttat ccatcccctg caaactgcag
                                                                              420
  158 agtggcactc attgcttgtg gacggaccag ctcctccaag gctctgaaaa gggcttccag
                                                                              480
  159 tecegteace ttgeetgeet geetegggag ceagggetgt geacetggea gteeetgegg
                                                                              540
                                                                              552
  160 tcccagatag cc
  162 <210> SEQ ID NO: 6
  163 <211> LENGTH: 184
```

Input Set : A:\36829-20002.00.txt

```
164 <212> TYPE: PRT
 165 <213> ORGANISM: Homo sapiens
 167 <400> SEQUENCE: 6
 168 Cys Thr Cys Val Pro Pro His Pro Gln Thr Ala Phe Cys Asn Ser Asp
 170 Leu Val Ile Arg Ala Lys Phe Val Gly Thr Pro Glu Val Asn Gln Thr
 171
 172 Thr Leu Tyr Gln Arg Tyr Glu Ile Lys Met Thr Lys Met Tyr Lys Gly
173
                                 40
174 Phe Gln Ala Leu Gly Asp Ala Ala Asp Ile Arg Phe Val Tyr Thr Pro
175
                             55
176 Ala Met Glu Ser Val Cys Gly Tyr Phe His Arg Ser His Asn Arg Ser
                         70
178 Glu Glu Phe Leu Ile Ala Gly Lys Leu Gln Asp Gly Leu Leu His Ile
179
                                         90
180 Thr Thr Cys Ser Phe Val Ala Pro Trp Asn Ser Leu Ser Leu Ala Gln
181
                100
                                     105
182 Arg Arg Gly Phe Thr Lys Thr Tyr Thr Val Gly Cys Glu Glu Cys Thr
            115
                                 120
184 Val Phe Pro Cys Leu Ser Ile Pro Cys Lys Leu Gln Ser Gly Thr His
                             135
186 Cys Leu Trp Thr Asp Gln Leu Leu Gln Gly Ser Glu Lys Gly Phe Gln
187 145
                        150
                                             155
188 Ser Arg His Leu Ala Cys Leu Pro Arg Glu Pro Gly Leu Cys Thr Trp
                    165
                                         170
190 Gln Ser Leu Arg Ser Gln Ile Ala
191
                180
193 <210> SEQ ID NO: 7
194 <211> LENGTH: 1525
195 <212> TYPE: DNA
196 <213> ORGANISM: Homo sapiens
198 <400> SEQUENCE: 7
199 totagaccat gtotggaaag totttcaagg coggtgtttg tocaccaaag aagtocgoto
                                                                             60
200 aatgtttgag atacaagaag ccagaatgtc aatccgactg gcaatgtcca ggtaagaaga
                                                                            120
201 gatgttgtcc agacacttgt ggtatcaagt gtctagaccc agttgacacc ccaaacccaa
                                                                            180
202 ctagaagaaa gccaggtaag tgtccagtta cttacggtca atgtttgatg ttgaacccac
                                                                            240
203 caaacttctg tgaaatggac ggtcaatgta agagagactt gaagtgttgt atgggtatgt
                                                                            300
204 gtggtaagtc ctgtgtttcc ccagtcaagg ccatggaaga ccctcaaggc gacgccgctc
                                                                            360
205 aaaaaaccga caccagtcat cacgaccaag accatccgac ttttaataaa attactccaa
                                                                            420
206 atttageega atttgetttt tetttgtata gacaattage teateaaagt aattetaeta
                                                                            480
207 acattttttt tagtcctgtt tctattgcca ctgctttcgc catgttgagt ttaggtacta
                                                                            540
208 aagccgatac ccatgacgag attttagaag gtttaaactt taatttgacc gaaatcccag
                                                                            600
209 aagcccaaat tcacgagggt tttcaagagt tgttgagaac tttgaatcaa cctgattctc
                                                                            660
210 aattgcaatt aactactggt aacggtttat ttttgtctga aggtttaaaa ttggttgaca
                                                                           720
211 aatteetaga agaegteaag aaactatate atagtgagge ttttacegtt aattttggtg
                                                                           780
212 atactgagga agctaaaaag caaattaatg attatgttga gaaaggcacc cagggtaaga
                                                                           840
213 tcgttgacct agttaaagaa ttagatcgtg ataccgtctt cgcactagtt aactatattt
                                                                           900
214 ttttcaaggg taagtgggaa cgtcctttcg aggttaaaga tactgaagag gaagattttc
                                                                           960
215 atgttgatca agttactact gtcaaagttc caatgatgaa aagactgggt atgttcaata
                                                                          1020
```

Input Set : A:\36829-20002.00.txt

| 217 218 219 220 221 222 223 224 226 227 228 | ttcaacattg caaaaaatta agttcttggg tcttattaat gaagtatta ggtaacgcta ctgctatttt tttttacca gacgaaggta agcttcaaca tttagagaat gagttgactc atgacattat tactaaattt ttagagaacg aggatcgtcg tagcgcttct ctgcacctgc caaagttaag tatcaccggt acttacgact taaaatctgt tttaggccag ttaggtatta ccaaagtttt ttctaacggt gccgatttga gtggtgttac tgaagaagct ccattaaaat tgagtaaagc tgttcacaaa gccgtcttaa ctattgatga aaagggtacc gaggccgccg gcgctatgtt cctggaagct attccaatga gcattccacc agaagttaaa tttaataaac cattcgtttt tctgatgatc gagcagaaca ctaaaagccc attgtttatg ggtaaggttg tcaacccaac tcagaagtag tcgac (210> SEQ ID NO: 8 (211> LENGTH: 503 (212> TYPE: PRT (213> ORGANISM: Homo sapiens | | | | | | | | | | 1080 1140 1200 1260 1320 1380 1440 1500 | | | | | | |
|---|---|-------------|-----------|-------|------|------|-------------|-----------|------------|----------|--|-------|--------------|--------------|-----|------------|--|
| 231 | 31 <400> SEQUENCE: 8 32 Met Ser Gly Lys Ser Phe Lys Ala Gly Val Cys Pro Pro Lys Lys Ser | | | | | | | | | | | | | | | | |
| | | Ser | Gly | Lys | Ser | Phe | Lys | Ala | Gly | Val | Cys | Pro | Pro | Lys | Lys | Ser | |
| 233 | | | | | 5 | | | | | 10 | | | | | 15 | | |
| | Ala | Gln | Cys | | Arg | Tyr | Lys | Lys | | Glu | Cys | Gln | Ser | | Trp | Gln | |
| 235 | G | D | 01 | 20 | Ť =- | * | G | G | 25 | 1 | m 1 | Q | 01 | 30 | T | 0 | |
| 236 | Cys | Pro | 35 | гÀг | ьуs | Arg | Cys | Cys 40 | Pro | ASP | THE | Cys | 45 | TTE | Lys | Cys | |
| | Τ.Δ11 | λen | | Va 1 | λen | Thr | Dro | | Dro | Thr | Δησ | Δνα | | Pro | Gly | Luc | |
| 239 | пеп | 50 | FIO | Val | кър | 1111 | 55 | NSII | FIO | 1111 | лгу | 60 | пуз | FIO | GIY | цуз | |
| | Cvs | | Val | Thr | Tvr | Glv | | Cvs | Leu | Met | Leu | | Pro | Pro | Asn | Phe | |
| 241 | _ | | | | -1- | 70 | 01 | 012 | | | 75 | | | | | 80 | |
| | | Glu | Met | Asp | Gly | Gln | Cys | Lys | Arg | Asp | Leu | Lys | Cys | Cys | Met | Gly | |
| 243 | - | | | _ | 85 | | - | _ | _ | 90 | | - | _ | _ | 95 | _ | |
| 244 | Met | Cys | Gly | Lys | Ser | Cys | Val | Ser | Pro | Val | Lys | Ala | Met | Glu | Asp | Pro | |
| 245 | | | | 100 | | | | | 105 | | | | | 110 | | | |
| | Gln | Gly | - | Ala | Ala | Gln | Lys | | Asp | Thr | Ser | His | | Asp | Gln | Asp | |
| 247 | | _ | 115 | -1 | _ | _ | | 120 | | . | | | 125 | 51. . | | n 1 | |
| | His | | Thr | Phe | Asn | Lys | | Thr | Pro | Asn | Leu | | GIu | Pne | Ala | Pne | |
| 249 | Cor | 130 | Пттт | λνα | Cln | Lou | 135 | uic | Cln | Cor | N c n | 140 | mh.∽ | λαη | Ile | Dho | |
| | 145 | neu | тут | ALY | GIII | 150 | Ата | птэ | GIII | 361 | 155 | 261 | 1111 | ASII | 116 | 160 | |
| | | Ser | Pro | Val | Ser | | Ala | Thr | Ala | Phe | | Met | Leu | Ser | Leu | | |
| 253 | | 001 | 110 | | 165 | | | | | 170 | | | 200 | 001 | 175 | 0-1 | |
| | Thr | Lys | Ala | Asp | | His | Asp | Glu | Ile | | Glu | Gly | Leu | Asn | Phe | Asn | |
| 255 | | - | | 180 | | | • | | 185 | | | • | | 190 | | | |
| 256 | Leu | Thr | Glu | Ile | Pro | Glu | Ala | Gln | Ile | His | Glu | Gly | Phe | Gln | Glu | Leu | |
| 257 | | | 195 | | | | | 200 | | | | | 205 | | | | |
| 258 | Leu | Arg | Thr | Leu | Asn | Gln | ${\tt Pro}$ | Asp | Ser | Gln | Leu | Gln | Leu | Thr | Thr | Gly | |
| 259 | | 210 | | | | | 215 | | | | | 220 | | | | | |
| | | Gly | Leu | Phe | Leu | | Glu | Gly | Leu | Lys | | Val | Asp | Lys | Phe | | |
| | 225 | | | _ | | 230 | _ | | a . | a ? | 235 | -1 | m1 | **. 1 | • | 240 | |
| | Glu | Asp | val | гàг | | Leu | туг | His | ser | | Ala | Pne | Thr | val | Asn | ьие | |
| 263 | c1 | λ ~~ | mb~ | C1 | 245 | | T *** | T *** | C1 ~ | 250 | 7.00 | λ c ~ | ™** ~ | นาไ | 255 | Tvc | |
| 265 | сту | wsb | TIII | 260 | GIU | WIG | пур | пÃ2 | 265 | TIG | หรม | кsр | TAT | 270 | Glu | пуз | |
| | Glv | Thr | Gln | | Lve | Tle | Val | Asn | | Val | Lvc | Glu | T.eu | | Arg | Asp | |
| 200 | - x | T 111 | 0111 | O T Y | 213 | 116 | , uı | 1135 | u | 141 | -73 | JIU | ⊥-cu | ".ab | A | .105 | |

RAW SEQUENCE LISTING ERROR SUMMARY PATENT APPLICATION: US/10/025,514 DATE: 04/22/2002 TIME: 16:20:22

Input Set : A:\36829-20002.00.txt

Output Set: N:\CRF3\04222002\J025514.raw

Use of n and/or Xaa have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the <220> to <223> fields of each sequence which presents at least one n or Xaa.

Seq#:12; Xaa Pos. 1,3,5

VERIFICATION SUMMARY

PATENT APPLICATION: US/10/025,514

DATE: 04/22/2002 TIME: 16:20:22

Input Set : A:\36829-20002.00.txt

Output Set: N:\CRF3\04222002\J025514.raw

L:14 M:270 C: Current Application Number differs, Replaced Current Application Number

L:15 M:271 C: Current Filing Date differs, Replaced Current Filing Date L:439 M:258 W: Mandatory Feature missing, <220> not found for SEQ ID#:12

L:440 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:12 after pos.:0